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Interdialytic weight gain and survival in hemodialysis patients: Effects of duration of ESRD and diabetes mellitus

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Background. Medical mortality determinants in end-stage renal disease (ESRD) patients treated with hemodialysis (HD) are well known. More recently, associations have been established between the dose of dialysis administered and patient survival. We showed in a prospective study that both dialyzer type and patient compliance with the dialysis prescription were independently associated with survival. Although several parameters of dialytic technique and patient compliance are associated with differential survival in patients with ESRD treated with HD, the association of interdialytic weight gain (IWG) with survival is unclear. No study has assessed the relationship between IWG and mortality in HD patients, controlled for multiple medical risk factors. The aim of our study was to determine whether IWG was associated with survival in patients with ESRD treated with HD, controlling for multiple medical and dialytic risk factors.

Methods. We prospectively conducted an observational, longitudinal, multicenter study of 283 urban HD patients to determine the relationship of IWG with several dialytic parameters and patient survival. Medical risk factors such as demographic indices and comorbid conditions were assessed. We studied Kt/V, the protein catabolic rate (PCR), serum albumin and anthropometric measurements, behavioral compliance indices, dialyzer characteristics, and serum electrolyte concentrations, and correlated these with IWG. In addition, the duration of dialysis was assessed in HD patients with and without diabetes mellitus. Cox proportional hazards models assessed the relative mortality risk of increased IWG, controlling for variations in medical comorbidity and other mortality determinants.

Results. The mean ($\pm$SD) age of our population was 54.6 $\pm$ 14.1 years, and the mean time they were treated with HD was 30.4 $\pm$ 46.9 months. The mean IWG was 1.54 $\pm$ 0.71% dry wt/day. Correlations were found between increased IWG and younger age, and lower midarm circumference, and increased Kt/V, PCR, and serum potassium concentration. The mean follow-up period was 48.9 $\pm$ 10.6 months. An increase in IWG was associated with a significantly increased relative mortality risk in diabetic ESRD patients treated with HD when variations in age, comorbidity, serum albumin concentration, and dialyzer type and site were controlled. There was, however, no association of increased mortality risk with increased IWG in the larger population of patients without diabetes. In further analyses, the increased mortality risk associated with increased IWG was found to be present only in patients with diabetes mellitus who had recently started HD therapy for ESRD.

Conclusion. IWG is correlated with several nutritional and dialytic variables and with parameters that predict survival in HD patients. Increased IWG is independently associated with decreased survival of diabetic ESRD patients treated with HD, after adjusting for variation in other medical risk factors. The population of incident diabetic HD patients is particularly susceptible to increased risk associated with increased IWG. The mechanisms underlying these results are obscure, but IWG might be associated with poorer survival in this population if it were linked to worsened hypertension, cardiovascular stress, or poorer glycemic control. Interventions to improve compliance with IWG in incident diabetic HD patients are warranted.

Key words: weight gain, ESRD, chronic renal disease, survival on hemodialysis, anthropometry.

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Compliance of HD patients is multifactorial and depends in large part on its defining parameters. To date, investigators in this field have not been able to agree on an index to serve as a gold standard for its measurement [1]. Compliance in this population depends on the extent to which an individual's behavior corresponds with the medical team's advice regarding dietary restrictions, medication regimens, and dialysis schedules [1]. As such, it can be measured by both subjective and objective indices, but compliance is difficult to assess with certainty [1–7]. Behavioral compliance has been associated with survival [7, 8], but the mediators of the effect have been poorly understood [2, 8]. We recently established quantitative measures to assess the effect of patients' shortening and skipping treatments, compared with physicians' prescribed times, and showed that these were often unrelated to standard biochemical compliance measures used to evaluate HD patients [2, 3, 8, 9]. Few studies have assessed the relationship between behavioral compliance measures and other factors, but older patients and Caucasian patients in several U.S. studies exhibited improved behavioral compliance [1, 3].

Because of the complexity of this parameter, several other factors besides the behavioral measurements previously mentioned have been considered as HD compliance markers, such as interdialytic weight gain (IWG), serum phosphate and potassium concentrations, patient's protein ingestion measured by protein catabolic rate (PCR), and adequacy of dialysis treatment. Unfortunately, each of these variables may be influenced by factors unrelated to compliance with prescribed medical and dietary regimens. Residual renal function, dialytic technique, drugs, and interactions among them can all affect their measurements [2, 3, 9].

Interdialytic weight gain is considered another measurement of compliance because it may be dictated, at least in part, by patient behavior. The role of IWG in determining survival is unclear. A recent study reported that HD patients who had greater than a 5.7% intersession IWG had a 35% higher risk of death, greater than the risk of death for skipping or shortening HD sessions [7].

The medical determinants of mortality in patients with end-stage renal disease (ESRD) treated with hemodialysis (HD) have been well delineated, consisting of demographic factors, the presence of diabetes mellitus, serum albumin levels, dose of dialysis administered, and comorbid conditions [8, 10–17]. Most of these factors have also been associated with IWG [1, 3, 18–20]. It has been unclear whether deleterious effects of IWG are associated with the presence of diabetes mellitus in this population [21, 22].

To determine whether IWG was associated with survival in patients with ESRD treated with HD, we prospectively examined the predictive power of IWG to predict mortality, after controlling for multiple medical and dialytic risk factors in patients with ESRD treated with HD, with and without diabetes mellitus.

METHODS

Patient population and demographics

We prospectively conducted an observational, longitudinal multicenter study of urban HD patients. Patient recruitment, limited to three HD centers in Washington, D.C., began September 1, 1992, and concluded April 1, 1996. All of the patients enrolled in chronic ESRD HD programs at the George Washington University Medical Center's Ambulatory Dialysis Unit (GWUMC), Howard University Medical Center's Dialysis Unit (HUMC), and the Washington Veterans Affairs Medical Center Dialysis Unit (VAMC), all in Washington D.C, with the exception of HIV-infected patients, patients who had a psychiatric diagnosis of psychosis, and patients who failed a minimental status exam, were eligible for the study. The follow-up ended December 31, 1997. Written informed consent was obtained at GWUMC and HUMC. Verbal consent was obtained prior to patients' enrollment at the VAMC. The study was approved by the institutional review boards of the three medical centers. Details regarding our recruitment procedures have been previously reported [3]. Two hundred eighty-three patients had serial measurements of IWG and continuous determinations of updated dry weight. In our recruitment planning, incident patients were defined as those who had commenced renal replacement therapy with HD less than six months at the time of study entry [9]. Prevalent patients were defined as those who had commenced renal replacement therapy with HD for more than six months at the time of study entry [8]. The demographics of our patient population are shown in Table 1.

Measures

Medical risk factors. Disease severity was determined by the ESRD severity coefficient of Plough et al, which was previously validated in a large sample of ESRD patients [17] and in our earlier studies [8]. The product of the patients' age and the relative risk (RR) of additional medical illness, such as cardiovascular and cerebrovascular disease, diabetes mellitus, collagen vascular disease, and malignancy, was used to derive the coefficient [8, 17], an overall measure of the level of severity of the patient's renal and comorbid chronic illnesses. In order to assess the possible effects of residual renal function on survival, the duration of ESRD therapy was used as a surrogate, as previous studies have shown that the glomerular filtration rate decreases as the course of therapy with HD continues [23].

Nutritional and anthropometric variables. PCR and the mean of three sequential monthly predialysis serum albumin, potassium, and phosphate concentrations after enrollment were determined. The midarm circumference (MAC) and arm muscle area (AMA) measurements were obtained by trained personnel at study entry, as previously described [3, 8, 9, 24, 25]. The percentage of ideal weight was calculated according to reference standards obtained from healthy adults during the National Health and Nutrition Examination Surveys (NHANES II), previously used in HD populations [26].

Dialytic parameters

Interdialytic weight gain was calculated as the patients' weight at the beginning of each HD session (preweight) minus the weight after (postweight) the previous HD session, divided by the nephrologists' determined dry

Table 1. Demographics of the hemodialysis (HD) patients studied

	Total population (N = 283)	Patients with DM (N = 119)	Patients without DM (N = 164)
Age *years*	54.6 ± 14.1	59.0 ± 11.3	51.4 ± 14.9[b]
Range	19–84	26–84	19–83
Gender			
Male	71.4% (N = 202)	73.9% (N = 88)	69.5% (N = 114)
Female	28.6% (N = 81)	26.1% (N = 31)	30.5% (N = 50)
Race			
African American	91.9% (N = 260)	96.6% (N = 115)	88.4% (N = 145)[a]
White and others	8.1% (N = 23)	3.4% (N = 4)	11.6% (N = 19)
Incident patients	39.9% (N = 113)	43.7% (N = 52)	37.2% (N = 61)
Prevalent patients	60.1% (N = 170)	56.3% (N = 67)	62.8% (N = 103)

All values are expressed as mean ± SD or percent. DM is diabetes mellitus.
[a]P = 0.003, [b]P = 0.0001, patients with and without diabetes mellitus

weight, divided by the interdialytic period in days, expressed as the percentage of change per day (%/d). IWG was calculated on the basis of the average of all measurements over a three-month period, beginning with the date of study entry. The value for dry weight was continuously updated according to nephrologists' changes in orders throughout the study.

Kt/V was assessed monthly at GWUMC and HUMC and quarterly at VAMC using the percentage of urea reduction (URR), as outlined by Jindal, Manuel, and Goldstein [3, 8, 9, 27]. The dialyzer used in each patient's treatment at study entry was noted and categorized as unmodified cellulose, modified cellulose, or synthetic according to the scheme of Hakim et al [8, 16].

Behavioral compliance. Behavioral compliance indices were collected for three months after the study entry. Individual rates of shortening, skipping, and integrated total time compliance were calculated. Patients' behavioral compliance with their prescribed HD regimen was assessed as previously described [3, 8, 9]: (*1*) The percent time compliance (%TCOMP) consisted of the amount of time the patient was actually dialyzed compared with the time physicians prescribed, only for sessions attended by the patient. This quantifies the time patients may decrease the length of dialysis sessions, characterizing "shortening" behavior. (*2*) The percent attendance (%ATTEND) comprised the number of sessions attended compared with the number prescribed, quantitating the percentage of sessions from which the patient was absent without excuse (such as being hospitalized or receiving treatment as a transient patient in another unit), characterizing "skipping" behavior. (*3*) The total time of compliance (%TTC) reflects the fraction of time the patient received dialysis compared with the total time prescribed in both attended and unattended sessions. This is an overall measure of compliance with the dialysis prescription, including "skipping" and "shortening" behaviors. The resulting values were averaged over a three-month period, beginning with the date of study entry. Individual behavioral compliance measures are highly stable over time [3, 8].

Statistical methods

All of the behavioral compliance data displayed highly positively skewed distributions. Correlations between demographic data, medical risk factors, nutritional and anthropometric variables, dialytic parameters, and compliance factors were assessed by Pearson's correlation coefficients or Spearman's rank order correlation coefficients, in the cases of skewed distribution of data, as previously described [3, 8, 9]. Differences between groups were assessed by unpaired *t*-tests, the Wilcoxon test, chi-square analysis, and analysis of variance (ANOVA), as appropriate [3, 8, 9].

Survival time for each patient was determined both by the number of days between date of initial study evaluation and the end of the study observation period or date of death, and the number of days from the start of ESRD therapy to the end of the study observation period or the patient's death. In addition, analyses were conducted evaluating survival from 90 days after the study entry until the end of the study observation period or date of death. Survival status was confirmed using the Health Care Finance Administration database, obtained through ESRD Network 5 (Richmond, VA, USA) for all patients enrolled in the study. Cox proportional hazards regression was used to predict mortality hazard [28]. Following the results of initial bivariate Cox regressions with selected demographic and dialytic indices [8], regression analyses were performed in the whole HD population, in the groups of diabetic and nondiabetic HD patients, in incident and prevalent populations, and in incident and prevalent populations with and without diabetes mellitus. The relationship between IWG and survival was examined in these groups while simultaneously controlling for predictor medical risk factors (patients' age, severity coefficient, level of serum albumin concentration, dialyzer type, and dialysis site) [8]. To determine whether there was a nonlinear relationship between survival and IWG, both IWG and patients' predialysis weights were stratified into quartiles, and regressions were performed in each of these subgroups. RRs or hazards, as outlined in text and tables, represent the expected change in mortality risk associated with a 1% increase in IWG. Analyses were performed using PROC PHREG in SAS 6.12 (SAS Institute Inc., Cary NC, USA) using the exact method for ties. The α level of tests of survival and group differences was 0.05. Data are presented as mean ± SD.

RESULTS

Population description

The total enrolled sample surveyed who had baseline assessment of dialytic and behavioral compliance measures and IWG comprised 283 subjects. African Americans comprised 91.9% ($N = 260$) of our patient population (Table 1). Eighty-one (28.6%) of the patients were female, and 119 (42%) had diabetes mellitus (Table 1). One hundred thirteen (39.9%) of the patients were incident to ESRD, and 170 (60.1%) were prevalent. Forty-six percent of the incident and 39.4% of the prevalent patients had diabetes mellitus (data not shown). There was no difference between the proportions of incident and prevalent patients with diabetes.

The mean age of our patient population was 54.6 ± 14.1 years (Table 1). Patients had been treated with HD for mean and median times of 30.4 ± 46.9 and 12.7 months, respectively, at the time of study enrollment (Table 2). The patients' mean serum albumin concentration was 3.8 ± 0.49 g/dL. The patients' mean predialysis weight was 73.9 ± 17.5 kg (data not shown). In the 210 patients (74.2%) in whom the percentage of ideal weight was assessed, the mean value was 102.1 ± 22.8%. Anthropometric evaluations were performed in 237 of the subjects (83.7%). Anthropometry could not be performed in 46 subjects because of disability associated with cerebrovascular disease, refusals, transfers from the unit, or death before assessment. The mean MAC and AMA were 25.8 ± 4.2 cm and 545.6 ± 182.1 mm^2, respectively. These findings suggest the patients had comparable nutritional status to a normative cohort of patients with ESRD treated with HD [26]. The patients' baseline mean PCR was 1.06 ± 0.27 g/kg/day. The mean URR was 0.60 ± 0.092 (data not shown), and the mean Kt/V was 1.2 ± 0.4. These values are comparable to those delineated in the ESRD Core Indicator Project, monitoring U.S. ESRD HD patients from the period of 1992 through 1995, when URRs ranged from 0.63 ± 0.097 to 0.64 ± 0.089 (personal communication, Drs. Pamela Frederick and Diane Frankenfield, Health Care Financing Administration, Baltimore, MD, USA), and the mean Kt/V demonstrated in special studies by the

Table 2. Clinical characteristics of the HD patients studied

	Total population (N = 283)	Patients with DM (N = 119)	Patients without DM (N = 164)	P	Incident patients (N = 113)	Prevalent patients (N = 170)	P
Duration of ESRD at study entry *months*	30.4 ± 46.9	6.19 ± 36.8	27.2 ± 55.3	<0.0001	2.1 ± 1.3	49.6 ± 52.7	<0.0001
Serum albumin *g/dL*	3.8 ± 0.49	3.77 ± 0.5	3.88 ± 0.4	0.062	3.69 ± 0.51	3.93 ± 0.44	0.0001
Kt/V	1.2 ± 0.4	1.18 ± 0.3	1.2 ± 0.3	0.104	1.10 ± 0.33	1.30 ± 0.29	0.0001
PCR *g/kg/day*	1.06 ± 0.27	1.04 ± 0.3	1.08 ± 0.3	0.304	0.95 ± 0.25	1.13 ± 0.26	0.0001
Serum K concentration *mEq/L*	4.8 ± 0.8	4.68 ± 0.5	4.87 ± 0.8	0.038	4.56 ± 0.56	4.94 ± 0.83	0.0001
Serum P concentration *mg/dL*	5.6 ± 1.7	5.49 ± 1.7	5.73 ± 1.7	0.268	5.21 ± 1.56	5.91 ± 1.82	0.0008
Behavioral compliance							
%TCOMP (time compliance)	97.8 ± 2.8	97.8 ± 3.1	97.9 ± 2.6	0.87	98.5 ± 2.4	97.4 ± 3.0	<0.01
%ATTEND (attendance)	98.4 ± 5.7	99.0 ± 3.7	97.9 ± 6.8	0.11	98.2 ± 7.2	98.6 ± 4.4	0.41
%TTC (total time compliance)	96.1 ± 6.6	96.8 ± 5.4	95.6 ± 7.4	0.15	96.5 ± 7.7	95.8 ± 5.9	0.75
Percent of ideal weight	102.1 ± 22.8	107.1 ± 20.5	98.7 ± 23.7	0.007	102.5 ± 22.1	102.0 ± 23.7	0.82
MAC *cm*	25.8 ± 4.2	26.3 ± 3.5	25.5 ± 4.7	0.09	26.4 ± 3.6	25.5 ± 4.6	0.39
AMA *mm*^{2}	545.6 ± 182.1	563.5 ± 148.3	532.8 ± 202.4	0.201	566.4 ± 156.1	534.1 ± 194.7	0.14
IWG *% dry weight/day*	1.54 ± 0.71	1.47 ± 0.6	1.59 ± 0.74	0.137	1.31 ± 0.65	1.70 ± 0.71	0.0001

Data are mean ± SD. Abbreviations are: HD, hemodialysis; IWG, interdialytic weight gain; K, potassium; P, phosphate; DM, diabetes mellitus; PCR, protein catabolic rate; MAC, mean arm circumference; AMA, arm muscle area.

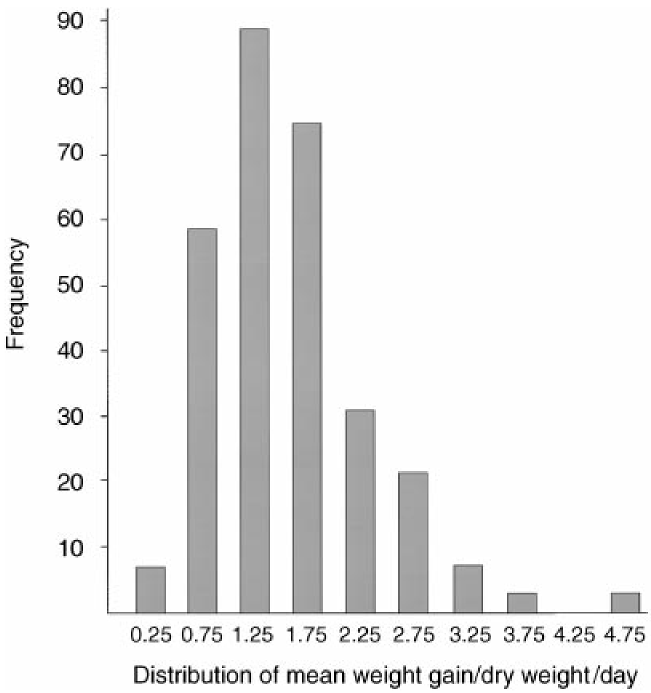

Fig. 1. Distribution of mean interdialytic weight gain (IWG) in 283 stable patients with end-stage renal disease (ESRD) treated with hemodialysis (HD). IWG was calculated as the patients' weight after each HD session, divided by determined dry weight, divided by the interdialytic period in days, expressed as a percentage of change per day (%/day). IWG was calculated on the basis of the average of all measurements over a three-month period, during which dry weight was continuously updated from physicians orders.

USRDS for 1993 was 1.1 (personal communication, Dr. L. Agodoa, NIDDK, NIH, Bethesda, MD, USA). Forty-three of the patients were treated with unmodified cellulose, 12.6% with modified cellulose, and 44.4% with synthetic dialyzers.

Behavioral compliance data were available for all of the patients. %TCOMP was 97.8 ± 2.8%, with a range of 86.3 to 100%. The mean %ATTEND was 98.4 ± 5.7%, with a range of 38.8 to 100%, and the mean %TTC was 96.1 ± 6.6%, with a range of 36.4 to 100%. These averages are comparable to those previously reported by others [29, 30].

The patients' mean predialysis serum potassium concentration was 4.8 ± 0.8 mEq/L, and the mean predialysis serum phosphate concentration was 5.6 ± 1.7 mg/dL.

Interdialytic weight gain

The mean IWG was 1.54 ± 0.71% dry weight/day (Table 2) (range 0.23 to 4.61%). Distribution of IWG showed a moderate skew (1.04; Fig. 1). The median value of IWG was 1.44% dry weight/day, and 90% of the values were lower than 2.57% dry weight/day (Fig. 1). The mean IWG was lower in patients treated with synthetic (1.42 ± 0.67% dry weight/day) compared with those treated with cellulose dialyzers (1.63 ± 0.73% dry weight/day, P = 0.01; data not shown). There was no significant association of IWG and patient gender. There was no difference in mean IWG between patients with and without diabetes mellitus, or between men and women, or between African Americans and patients of other ethnic backgrounds (data not shown).

Table 3. Correlation matrix of variables with IWG in ESRD patients treated with HD with and without DM

	Total population (N = 283)		Patients with DM (N = 119)		Patients without DM (N = 164)	
	r	P	r	P	r	P
Age	−0.16	0.004	−0.24	0.009	−0.108	0.16
Gender	−0.01	0.89	0.08	0.38	−0.07	0.37
Race	−0.06	0.29	−0.09	0.29	−0.04	0.64
Serum albumin	−0.11	0.06	−0.1	0.28	−0.14	0.07
PCR	0.25	0.0001	0.22	0.02	0.26	0.001
Kt/V	0.19	0.002	0.24	0.01	0.14	0.08
%IW	−0.24	0.0004	−0.09	0.44	−0.31	0.0005
MAC	−0.13	0.05	−0.23	0.02	−0.07	0.43
AMA	−0.11	0.08	−0.21	0.04	−0.06	0.49
Serum K	0.21	0.0003	0.18	0.38	0.22	0.006
Serum P	0.07	0.25	0.076	0.41	0.06	0.47
%TCOMP[a]	−0.13	0.02	−0.19	0.04	−0.09	0.25
%ATTEND[a]	0.05	0.36	0.02	0.79	0.08	0.29
%TTC[a]	−0.05	0.37	−0.06	0.47	−0.03	0.72

Abbreviations are: IWG, interdialytic weight gain; %IW, percentage of ideal weight; PCR, protein catabolic rate; MAC, mean arm circumference; AMA, arm muscle area; K, potassium; P, phosphate; DM, diabetes mellitus; %TCOMP, percent time compliance; %ATTEND, percent attendance; %TTC, total time compliance (see text for details).

[a]Spearman correlation; all other correlations are Pearson correlation coefficients

Increased IWG was associated with younger patient age (r = −0.16, P = 0.004) and higher Kt/V and PCR (r = 0.19, P = 0.002, and r = 0.25, P = 0.0001, respectively; Table 3). IWG inversely correlated with patients' predialysis weight (r = −0.24, P = 0.0003; data not shown). IWG inversely correlated with MAC (r = −0.13, P = 0.05) and with the percentage of ideal weight (r = −0.24, P = 0.0004), but not with AMA (r = −0.11, P = 0.08). IWG correlated with mean serum potassium concentration (r = 0.21, P = 0.0003), but not with mean serum phosphate concentration (r = 0.07, P = 0.25). The correlation between increased IWG and lower serum albumin concentration approached but did not reach a level of statistical significance (r = −0.11, P = 0.06). Increased IWG was inversely correlated with worsened shortening behavior (r = −0.13, P = 0.02, Spearman test), but there was no correlation of patients' IWG and level of attendance, total integrated time compliance (Table 3), or dialyzer type used in treatment (data not shown).

Associations with duration of end-stage renal disease therapy

There was no difference in the mean age or severity coefficient between incident and prevalent patients (data not shown). Incident patients were treated with HD for a mean of 2.1 ± 1.3 months at the time of study entry, compared with 49.6 ± 52.7 months for prevalent patients ($P < 0.0001$; Table 2). In prevalent patients, IWG correlated inversely with patients' predialysis weight ($r = -0.24$, $P = 0.0035$), but there was no significant correlation of the variables in incident patients ($r = -0.18$, $P = 0.12$), perhaps in part because of the smaller number of subjects (data not shown). There was a significant correlation between IWG and the number of days the patient had been treated for ESRD with HD at the time of study entry ($r = -0.165$, $P = 0.0045$; data not shown). There were, however, no correlations of IWG and duration of HD therapy for ESRD prior to study entry in incident patients ($r = -0.074$, $P = 0.44$), prevalent patients ($r = 0.055$, $P = 0.48$), prevalent patients without diabetes mellitus ($r = 0.0077$, $P = 0.44$), prevalent patients with diabetes mellitus ($r = -0.0077$, $P = 0.54$), incident patients without diabetes mellitus ($r = -0.10$, $P = 0.43$), and incident patients with diabetes mellitus ($r = -0.03$, $P = 0.81$; data not shown).

As in previous interim analyses in this patient population [9], incident patients had significantly lower mean Kt/V, PCR and serum albumin, potassium, and phosphate concentrations compared with prevalent patients (Table 2). Incident patients had a significantly lower IWG than prevalent patients (1.31 ± 0.65 vs. 1.70 ± 0.71% dry wt/day, $P = 0.0001$). There was no difference between the mean levels of anthropometric indices of incident and prevalent patients.

There were similar statistically significant correlations between IWG and age, Kt/V and PCR, MAC and serum potassium concentration in the prevalent patient population (compared with the whole patient population of 283 patients outlined in Table 3; data not shown). In contrast to the whole population, there was no correlation of IWG and duration of dialysis, serum phosphate concentration, or shortening behavior in the prevalent patients (data not shown). There were no similar statistically significant correlations between IWG and other demographic, biochemical, or compliance measures in the incident patients, with the exception of the correlation of IWG and serum albumin concentration ($r = -0.32$, $P = 0.0007$; data not shown).

Associations with diabetes mellitus

There was no significant association between the presence of diabetes mellitus and changes in IWG. The only differences between patients with and without diabetes mellitus were that patients with diabetes were treated for ESRD for a shorter period of time at the study entry, they had lower mean serum potassium concentrations, and they had a higher percentage ideal body weight (Table 2).

Incident diabetic patients were older and had significantly lower mean serum albumin concentrations and Kt/V compared with incident non-diabetic patients, but there were no differences between the two groups in the mean percentage ideal weight, IWG, PCR, serum phosphate or potassium concentration, or anthropometric indices (data not shown). Prevalent diabetic patients were older and had a higher mean percentage of ideal weight and MAC than prevalent non-diabetic patients, but there were no differences between the two groups in mean IWG, PCR or Kt/V, serum albumin, phosphate or potassium concentrations, or AMA (data not shown).

There were a few differences between significant correlations in patients with and without diabetes compared with the population as a whole. In patients with diabetes mellitus, there was no correlation of percentage ideal weight or serum potassium concentration with IWG. The correlation between IWG and patients' predialysis weight approached the level of statistical significance in patients with diabetes ($r = -0.20$, $P = 0.06$), but it was significant in the population without diabetes ($r = -0.25$, $P = 0.0035$; data not shown). In patients without diabetes mellitus, no correlations between IWG and age, Kt/V, MAC, AMA, or shortening behavior were found (Table 3). There was no correlation between IWG and patients' predialysis weight ($r = -0.12$, $P = 0.48$) in the small group of incident patients with diabetes (data not shown).

Survival analyses

The mean follow-up time was 48.9 ± 10.6 months (range 20.9 to 60.5 months). A Cox regression applied to the entire sample confirmed, as expected, a significantly increased mortality risk for each decade increase in age, each unit increase in severity coefficient, and each decrease in serum albumin concentration, as previously described [8].

Finally, the effects of variation in IWG were tested. Patients' age, severity coefficient, level of serum albumin concentration, and dialyzer type and site were entered in the Cox regression first and thus controlled for prior to analysis. In the whole HD population, an increase in IWG was not associated with a significant increase in RR, when variations in age, severity of illness, serum albumin concentration, and dialyzer type and site were controlled (RR 1.24, $P = 0.14$; Table 4). In the nondiabetic HD patients, increased IWG was also not associated with an increased RR after controlling for the previously mentioned factors (RR 0.913, $P = 0.65$). In HD patients with diabetes mellitus, there was, however, a significant association between increased IWG and mortality. For each 1% increase in IWG, there was a 67.5% increase in relative mortality risk, after controlling for other factors (RR 1.675, $P = 0.01$; Table 4). There was no significant increase in relative mortality risk associated with increased IWG in incident or prevalent subpopulations (Table 4). While there was no increased

Table 4. Survival analysis: Predicting mortality by Cox regression analysis, using IWG in different ESRD populations, after controlling for medical risk factors

Population	*N*	RR	95% CI	*P*
ESRD HD population	283	1.24	0.93–1.64	0.14
ESRD HD patients without DM	164	0.913	0.61–1.36	0.65
ESRD HD patients with DM	119	1.675	1.12–2.51	0.01
ESRD incident HD patients	113	1.39	0.82–2.36	0.23
ESRD incident HD patients with DM	52	2.9	1.14–7.4	0.025
ESRD incident HD patients without DM	61	0.77	0.325–1.82	0.55
ESRD prevalent HD patients	170	0.9	0.62–1.32	0.59
ESRD prevalent HD patients with DM	67	1.15	0.68–1.95	0.61
ESRD prevalent HD patients without DM	103	0.672	0.40–1.13	0.13

Abbreviations are: IWG, interdialytic weight gain; ESRD, end-stage renal disease; HD, hemodialysis; DM, diabetes mellitus; RR, risk ratio; CI, confidence interval. RRs refer to 1% increase per dry weight per day (details are in the text).

relative mortality risk associated with increased IWG in prevalent patients with diabetes mellitus, there was a 190% increase in relative mortality risk in the subset of incident patients with diabetes mellitus (RR 2.90, CI 1.14 to 7.4, $P = 0.025$). Similar findings were noted when Cox analyses were performed in the subset of incident patients with diabetes mellitus, assessing patient survival from the start of ESRD therapy with HD (RR 3.05, CI 1.19 to 7.8, $P = 0.021$). There were no differences in interpretation of findings when survival analyses started at the end of the three-month initial data collection period.

In the whole HD population and in the subset of diabetic HD patients, an association of increased mortality risk with predialysis weight or IWG could not be demonstrated when stratification of these variables was used in Cox regression equations (data not shown).

DISCUSSION

Several different lines of evidence suggest that compliance with dietary and medical regimens [7, 8, 12] of patients with ESRD treated with HD is associated with outcomes, such as survival. However, compliance is clearly a multifactorial concept that involves at least several types of behavior: adherence to several different types of fluid and dietary restrictions, medication regimens, and treatment schedules [1, 2, 9]. The complexity of the dimensions of compliance, the lack of a clear gold standard for its measurement, and the multiple factors involved in determining the survival of the HD population also make it difficult to assess. Among the multiple measurements that have been used to estimate the compliance of HD patients, we used objective parameters such as IWG and quantitated measures of patients' shortening and skipping behaviors, and integrated total behavioral compliance, and analyzed their interrelations with HD survival risk factors.

Interdialytic weight gain is primarily determined by the HD patients' fluid and sodium ingestion, but factors such as hyperglycemia and hyperosmolality, residual renal function, and extent of urine output may be nonbehaviorally related factors affecting IWG [9]. The mean duration of ESRD therapy at the time of enrollment in our patient population was 30 months, and it is therefore unlikely that the majority of patients maintained a substantial urine output at this point. Since studies have demonstrated that residual renal function in HD patients decreases as duration of ESRD therapy increases [23], we used both their duration of HD and epidemiologic status as surrogates for this parameter. Because of our sampling strategies, there was a marked difference between the duration of ESRD therapy in incident and prevalent patients (2 months vs. 4 years). It is similarly unlikely that there was clinically significant residual renal function in the prevalent subgroup in this study. Although there were lower levels of serum albumin concentration, Kt/V and PCR in incident compared with prevalent patients, demographic risk factors such as age, race, extent of comorbidity, and anthropometric indices were not different between the two groups. In accord with this strategy, lower levels of serum phosphate and potassium concentration, as well as IWG in the incident population, may reflect differences between residual renal function in these two subpopulations. Unfortunately, this parameter was not directly measured in our study.

Different studies have defined IWG and the level of IWG defined as noncompliant in various ways. Kaplan de Nour, in her multifaceted five-point scale, considered absolute values of IWG ranging from 0.5 kg to greater or equal to 2.5 kg [5]. Manley and Sweeney considered three measures of weight gain: absolute weight gain, the standard deviation of each patient's weight gain, and the ratio of weight gain to dry weight [6]. Agashua et al used the presession weight and two cut-off points (mean intersession weight gain of 1 and 1.5 kg, clinically determining the upper limits of dietary compliance) [31]. Leggat et al using the USRDS database defined noncompliance as greater than 5.7% of dry weight per interdialytic session [7]. It is not clear in the latter study whether data were normalized for sessions separated by a variable number of days. The wide variation among the different methods used to define the compliant values of IWG measurements and the lack of clear association with outcome measures have made it difficult to generalize when rating patients' compliance on this factor. In our study, we used a more accurate method to measure IWG. A percentage of IWG per day, accounting for the variability in interdialytic days between three-times weekly sessions over each month, was calculated using the average of measurements during a three-month period, with the nephrologists' dry weight continuously updated. This may be particularly important in incident patients, in whom dry weight may change during the early part of treatment, but may increase during later months of therapy, as recently outlined [32]. We correlated our continuous value of IWG with different parameters without considering a distinct cut-off. Only slightly more than 10% of our patients had an IWG comparable to that used as a mortality marker by Leggat et al [7]. This may account for some of the discrepancy between our findings. In addition, this group assessed a prevalent population, perhaps also accounting for some of the discrepancies in risk assessments between the two studies.

To assess patient's behavioral compliance, we used a three-month period to determine a score based on a scale that characterized "shortening" and "skipping" behaviors and an overall measure of compliance with the dialysis prescription, including "skipping" and "shortening" behaviors. We showed in previous reports that individual behavior compliance measures of patients' shortening, skipping, and integrated total time compliance are highly stable over time [3]. When correlating these variables with IWG, we found that shortening behavior was inversely correlated with IWG, but there was no correlation between IWG and the level of attendance or total integrated time compliance. These results may be explained by the dependence of IWG on fluid removal scheduled during a particular HD procedure (in effect predicating that shortening treatments leads to lower achieved ultrafiltration rates). In contrast, patients who skip sessions may voluntarily restrict interdialytic fluid intake.

Age has been a consistently strong predictor of compliance in many studies in ESRD patients [3, 7, 9, 31, 33, 34]. We and others have shown that younger patients are more likely to be noncompliant, whereas older patients are more likely to be compliant [2, 3, 7, 8]. In this study, we found that increased IWG was associated with younger patient age, supporting the usefulness and generalizability of our measure of IWG as a compliance behavior. This association, however, suggests that all analyses of the relationship between IWG and mortality must be controlled for age.

In a previous report, we showed that men were significantly more likely to be noncompliant, as measured by skipping or shortening HD sessions [3]. In the current study, however, there was no correlation of IWG and patient gender. Similar results were reported by Leggat et al [7]. The discrepancy between the finding of a correlation between gender and behavioral compliance in our earlier study and the lack of such an association in the present study may be due to the fact that the earlier study [3] was smaller and limited to only prevalent patients who had survived at least six months of dialytic therapy for ESRD.

The mean values of serum albumin concentration, PCR, and anthropometric measurements in our sample suggest that we studied a well-nourished population of HD patients [26]. In our patients, we found that IWG was correlated with PCR, and the inverse correlation between IWG and serum albumin concentration approached the level of statistical significance. These results are comparable to those found by other investigators. Testa and Beaud recently showed a positive correlation between IWG and PCR and serum albumin levels in 38 patients with ESRD treated with HD [20]. The group of patients with higher levels of mean IWG had a higher mean serum albumin concentration. In the same study, age was negatively correlated with both IWG and PCR, and the authors concluded that IWG was associated with better nutritional status. Sherman et al reported, in a large number of ESRD patients, that greater IWG is associated with a higher normalized PCR and showed a trend towards a positive correlation between levels of IWG and serum albumin [18]. They had, however, previously hypothesized an inverse relationship between these two variables (as found in the present study). They suggested the lack of significance (or an inverse correlation) might have been a function of dilution of predialysis serum albumin concentrations by increased total body water, as a result of noncompliance with fluid restrictions. We agree with this interpretation.

To our knowledge, no other studies have investigated the association of IWG and other parameters of nutritional status, such as anthropometric measurements. We analyzed these variables and found that IWG was inversely correlated with MAC and with the percentage of ideal weight. No correlation was found between IWG and AMA. These results do not support a robust association of IWG and nutritional status. The findings may be because anthropometric measurements are not sufficiently precise or may be misleading in patients with ESRD because of altered tissue hydration or myopathy. We recently reported preliminary findings showing that serum albumin concentration is a better prognostic marker than anthropometric measures in HD patients [35]. Other more sophisticated measures of body composition, such as bioelectrical impedance analysis, dual-energy x-ray absorptiometry, and total body nitrogen have been used as methods of nutritional assessment [36, 37], but their relationship to survival remains unknown in

HD patients. However, as with compliance measures, no gold standard exists for the nutritional evaluation of patients with ESRD treated with HD.

We found, as expected, that IWG was positively correlated with Kt/V and with the mean serum potassium concentration, but not with the mean serum phosphate concentration. Sherman et al found that Kt/V was higher in patients with high IWG as a percentage of dry weight, but could not demonstrate a significant correlation between the two variables in a large patient population [18]. Differences between our findings and theirs may be due to differences in evaluation of Kt/V. Morduchowicz et al, in a study of 50 patients, were unable to demonstrate a correlation of serum phosphate concentration and IWG [38]. Predialytic serum ion concentrations may be affected by multiple variables besides dietary intake, such as the effects of hemodilution, medications, residual renal function, hormonal status, and acid-base homeostasis [1, 2, 9]. Kt/V and serum potassium concentration have usually been linked with dialytic parameters and not generally used as compliance markers by themselves [2, 7, 12, 15, 16, 31]. In contrast, serum phosphate concentration has been used as a marker of both dietary and medication compliance, while its predialytic and postdialytic levels are not closely related to dialytic clearance [2, 7, 12, 30]. Lowrie and Lew [12] and we (unpublished data from this population) found that hyperphosphatemia is a mortality risk factor for HD patients. These findings further emphasize the lack of association we currently found between IWG and survival in patients without diabetes mellitus.

The relationship between IWG and type of dialyzer has not been reported in current studies of this subject. When using high-flux dialyzers, it is possible to remove large amounts of fluid, which can in turn determine changes in patients' osmolality and body volume that may affect interdialytic fluid intake. We analyzed patients' treatments with unmodified cellulose dialyzers with low ultrafiltration coefficients and modified cellulose and synthetic dialyzers with higher ultrafiltration coefficients [8]. In the present study there was no correlation of patient IWG and dialyzer type used for treatment, although there was a difference between mean IWG in patients treated with cellulose compared with synthetic dialyzers. These findings suggest that, although IWG is affected by several dialytic factors, the different effects determined by the type of dialyzer used in HD treatment are not intimately associated with variations in IWG. Such notions must, however, be assessed in carefully planned, multicenter, randomized, prospective controlled studies. It should be observed that the dialyzer type was controlled for in all survival analyses in this study.

It is important to note in any analysis of the association of IWG with survival that IWG had been correlated with several established mortality risk factors in HD patients. We observed a correlation of IWG with age, as others have. In addition, the correlation of IWG and serum albumin approached the level of statistical significance. IWG in our study was correlated with dialytic markers that have been found to be associated with survival in epidemiologic studies, such as Kt/V. IWG was correlated with a behavioral compliance measure, which we have previously shown to be associated with enhanced survival [8]. When relative mortality risk associated with variation in IWG was controlled for variation in age, severity of comorbid illness, serum albumin concentration, and dialyzer type, we were unable to show an association with survival in the whole population. In addition, there was little relationship between IWG and type of dialyzer used, which we [8] and others [16] have shown is a parameter associated with differential mortality. These findings and our analytic strategy suggest differences in IWG do not underlie the differential survival of HD patients treated with different types of dialyzers.

In this study, we show that diabetic ESRD patients treated with HD, who have greater morbidity and mortality than nondiabetic ESRD patients [10], are particularly susceptible to mortality when IWG is increased. Of note, although there were few differences between the two populations, the diabetic patients were more overweight and had a tendency to hypoalbuminemia. Although the percentage of the population studied with diabetes was substantial, no correlation was found between the presence of diabetes and IWG. Previous studies have suggested a relationship between increased IWG and poor glycemic control in ESRD patients with diabetes [21] and increased IWG in HD patients with diabetes mellitus [21]. The association we found between IWG and mortality in the diabetic HD population suggests that excessive IWG could be a contributory factor to progression of cardiovascular disease in patients already at risk [39].

Recent work has shown increased survival in a largely African American population with increased body mass index [40]. Our measure of IWG was normalized for dry weight. Although stratification analyses of predialytic weight and IWD in our relatively small population did not reveal associations with increased risk, increased IWG would be of greatest consequence in those incident diabetic patients with the lowest body mass indices.

Alternatively, increased IWG may be associated with poor glycemic control, which might also mediate poorer survival [21], or with any deleterious effects of hypertension. A link between level of blood pressure and outcome in HD patients has not been clearly established [reviewed in 41, 42]. A recent study in a large population of U.S. HD patients did not demonstrate an association of predialysis hypertension and mortality, and found no difference between outcomes regarding such parameters in diabetic and nondiabetic patients [41]. In their analyses, high presumptive IWG was not associated with a low blood pressure mortality effect. However, control of blood pressure, often with antihypertensive medications, has been shown to be associated with improved outcomes in European [43] and American patients [reviewed in 41 and 42]. The role of blood pressure or antihypertensive therapy [42] in association with outcome was unfortunately not assessed in this study. In patients with diabetes, worsened shortening behavior was associated with increased IWG. This may also be a mechanism whereby IWG mediates poorer outcome, as well as psychological differences between the groups [8].

A major weakness of the study is that residual renal function was not assessed directly. In order to evaluate this parameter indirectly, which is costly and cumbersome to measure in a large patient population, we analyzed our data according to predetermined categories of incidence and prevalence. There was a marked separation in duration of renal replacement therapy in these populations (but no difference between that of incident patients with and without diabetes). Studies have suggested that residual renal function falls as duration of ESRD therapy increases [23]. Surprisingly, the incident patients with diabetes, with presumably the highest levels of residual renal function, were at the greatest risk. This suggests that those diabetic patients who consume the most salt and water or who have the lowest glomerular filtration rates at the time of starting HD therapy or the swiftest loss of residual renal function are at greatest risk. Differences between findings in incident and prevalent groups may reflect survivor biases, but only in analyses of the latter group of patients. This points out that the findings in the incident patients are all the more important and epidemiologically valid, as it is unlikely that a survivor bias exists in this group. The mechanism underlying the findings, however, is incompletely explained. More definitive conclusions can be garnered by similar studies, powered by initial and longitudinal determinations of residual renal function, glycemic control, level of blood pressure, and changes in cardiac function, which were beyond the scope of these initial studies. Such investigations are, however, being performed or are in the planning stages.

A multicenter European study, with a comparable number of patients, was unable to document an association of IWG and increased mortality in patients with ESRD and diabetes [44]. Our population, in contrast, was largely composed of African American patients. It is not possible to compare the baseline demographics and risk factors between these two populations except for ethnic composition. In addition, we do not have information regarding the prevalence of such factors as smoking and left ventricular abnormalities in our population to compare with the European study. In addition, the European patients also had anthropometric indices consistent with malnutrition, but they were underweight. Differences in these factors or analytic approaches may account for this difference in study results. Moreover, our findings may not be generalizable beyond an urban, African American population. Further outcome studies must be performed addressing the association between IWG, glycemic control, and the incidence and prevalence of cardiovascular disease in larger populations of African American and other diabetic patients with ESRD treated with HD. This is particularly important because of the overrepresentation of African American patients in the U.S. ESRD program.

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REFERENCES

1. Lamping DL, Campbell KA: Hemodialysis compliance: Assessment, prediction and intervention. *Semin Dial* 3:105–111, 1990
2. Kobrin SM, Kimmel PL, Simmens SJ, Reiss D: Behavioral and biochemical indices of compliance in hemodialysis patients. *ASAIO Trans* 37:M378–M380, 1991
3. Kimmel PL, Peterson RA, Weihs KL, Simmens SJ, Boyle DH, Verme D, Umana WO, Veis JH, Alleyne S, Cruz I: Behavioral compliance with dialysis prescription in hemodialysis patients. *J Am Soc Nephrol* 5:1826–18341, 1995
4. O'Brien ME: Compliance and long-term maintenance dialysis. *Am J Kidney Dis* 15:209–214, 1990
5. Kaplan de-Nour A, Czaczkes JW: Personality factors in chronic hemodialysis patients causing noncompliance with medical regimen. *Psychosom Med* 34:333–334, 1972
6. Manley M, Sweeney J: Assessment of compliance in hemodialysis adaptation. *J Psychosom Res* 30:153–161, 1986
7. Leggat JE, Orzol SM, Hulbert-Shearon TE, Golper TA, Jones CA, Held PJ, Port FK: Noncompliance in hemodialysis: Predictors and survival analysis. *Am J Kidney Dis* 32:139–145, 1998
8. Kimmel PL, Peterson RA, Weihs KL, Simmens SJ, Alleyne S, Cruz I, Veis JH: Psychosocial factors, behavioral compliance and survival in urban hemodialysis patients. *Kidney Int* 54:245–254, 1998
9. Kimmel PL, Peterson RA, Weihs KL, Simmens SJ, Boyle DH, Umana WO, Kovac JA, Alleyne S, Cruz I, Veis JH: Psychologic

functioning, quality of life, and behavioral compliance in patients beginning hemodialysis. *J Am Soc Nephrol* 7:2152–2159, 1996
10. United States Renal Data System (USRDS): Excerpts from the United States Renal Data System 1996 Annual Report. Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive Diseases, 1996
11. Lowrie EG, Laird M, Parker TF, Sargent JA: The effect of hemodialysis prescription on patient mortality: Report from the NCDS. *N Engl J Med* 32:382–389, 1981
12. Lowrie EG, Lew NL: Death risk in hemodialysis patients: The predictive value of commonly measured variables and an evaluation of death rate differences between facilities. *Am J Kidney Dis* 15:458–482, 1990
13. Owen WF Jr, Lew NL, Liu Y, Lowrie EG, Lazarus JM: The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. *N Engl J Med* 329:1001–1006, 1993
14. Hakim RM, Breyer J, Ismail N, Schulman G: Effects of dose of dialysis on morbidity and mortality. *Am J Kidney Dis* 23:661–669, 1994
15. Held PJ, Port FK, Wolfe RA, Stannard DC, Carroll CE, Daugirdas JT, Bloembergen WE, Greer JW, Hakim RM: The dose of hemodialysis and patient mortality. *Kidney Int* 50:550–556, 1996
16. Hakim RM, Held PJ, Stannard DC, Wolfe RA, Port FK, Daugirdas JT, Agodoa L: Effect of the dialysis membrane on mortality of chronic hemodialysis patients. *Kidney Int* 50:566–570, 1996
17. Plough AL, Shwartz M, Salem SR, Weller JM, Ferguson CW: Severity analysis in end stage renal disease: A risk group approach. *Am Soc Artif Intern Org J* 8:33–40, 1985
18. Sherman RA, Cody RP, Rogers ME, Solanchick JC: Interdialytic weight gain and nutritional parameters in chronic hemodialysis patients. *Am J Kidney Dis* 25:579–583, 1995
19. Ifudu O, Chan E, Brezsnyak WF, Reydel C, McClendon E, Surgrue T, Di Rienzo M, Avram MM, Freidman EA: Interdialytic weight gain and missed dialysis treatments in long-term hemodialysis patients. *Dial Transplant* 24:292–303, 1995
20. Testa A, Beaud JM: The other side of the coin: Interdialytic weight gain as an index of good nutrition. *Am J Kidney Dis* 31:830–834, 1998
21. Ifudu O, Dulin AL, Friedman EA: Interdialytic weight gain correlates with glycosylated hemoglobin in diabetic hemodialysis patients. *Am J Kidney Dis* 23:686–691, 1994
22. Jones R, Poston L, Hinestrosa H, Parsons V, Williams R: Weight gain between dialyses in diabetics: Possible significance of raised intracellular sodium content. *Br Med J* 280:153, 1980
23. Lysaght M, Vonesh EF, Gotch F, Ibels L, Keen M, Lindholm B, Nolph KD, Pollack CA, Prowant B, Farrell PC: The influence of dialysis treatment modality on the decline of remaining renal function. *Trans Am Soc Artif Intern Org* 37:598–604, 1991
24. Durnin JVGA, Womersley J: Body fat assessed from total body density and its estimation from skinfold thickness: Measurements on 481 men and women aged from 16 to 72 years. *Br J Nutr* 32:77–96, 1974
25. Heymsfield SB, McManus C, Smith J, Stevens V, Nixon DW: Anthropometric measurement of muscle mass: Revised equations for calculating bone-free arm muscle area. *Am J Clin Nutr* 36:680–690, 1982
26. Nelson EE, Changgi DH, Pesce AL, Peterson DW, Singh S, Pollack VE: Anthropometric norms for the dialysis population. *Am J Kidney Dis* 6:32–37, 1990
27. Jindal JK, Manuel A, Goldstein MB: Percent reduction in blood urea concentration during hemodialysis. *Trans Am Soc Artif Intern Organs* 33:286–288, 1987
28. Lee EL: *Statistical Methods for Survival Data Analysis* (2nd ed). New York, Wiley, 1992, pp 250–263
29. Rocco MV, Burkart JM: Prevalence of missed treatments and early sign offs in hemodialysis patients. *J Am Soc Nephrol* 4:1178–1183, 1993
30. Sherman RA, Cody RP, Matera JJ, Rogers ME, Solanchick JC: Deficiencies in delivered hemodialysis therapy due to missed and shortened treatments. *Am J Kidney Dis* 24:921–923, 1994
31. Agashua PA, Lyle RC, Livesley WJ, Slade PD, Winney RJ, Irwin M: Predicting dietary non-compliance of patients on intermittent hemodialysis. *J Psychosom Res* 25:289–301, 1981
32. Chazot C, Charra B, Vo Van C, Jean G, Vanel T, Calemard E, Terrat JC, Ruffet M, Laurent G: The Janus-faced aspect of dry weight. *Nephrol Dial Transplant* 14:121–124, 1999
33. Gonsalvez-Ebrahim L, Sterin G, Gulledge AD, Gipson WT, Rodgers DA: Noncompliance in younger adults on HD. *Psychosomatics* 28:34–41, 1987
34. McKevitt PM, Jones JF, Lane DA, Marion RR: The elderly on dialysis: Some considerations in compliance. *Am J Kidney Dis* 16:346–350, 1990
35. Kimmel PL, Simmens S, Veis J, Mishkin G, Cruz I: Serum albumin concentration predicts survival better than anthropometric indices in hemodialysis patients. *J Am Soc Nephrol* 9:A1089, 1998
36. Chertow GM, Lowrie EG, Wilmore DW, Gonzalez J, Lew NL, Ling J, Leboff MS, Gottlieb MN, Huang W, Zebrowski B, College J, Lazarus JM: Nutritional assessment with bioelectrical impedance analysis in maintenance hemodialysis patients. *J Am Soc Nephrol* 6:75–81, 1995
37. Pollock CA, Ibels LS, Allen BJ, Ayass W, Caterson RJ, Waugh DA, Macadam C, Pennock Y, Mahony JF: Total body nitrogen as a prognostic marker in maintenance dialysis. *J Am Soc Nephrol* 6:82–88, 1995
38. Morduchowicz G, Sulkes J, Aizic S, Gabbay U, Winkler J, Boner G: Compliance in hemodialysis patients: A multivariate regression analysis. *Nephron* 64:365–368, 1993
39. Culleton BF, Wilson PWF: Cardiovascular disease: Risk factors, secular trends, and therapeutic guidelines. *J Am Soc Nephrol* 9(Suppl):S5–S15, 1998
40. Fleischman E, Teal N, Dudley J, May W, Bower D, Salahudeen A: Overweight in hemodialysis and its influence on mortality and hospital stay: Data from 1,346 patients. *Kidney Int* 55:1560–1567, 1999
41. Port FK, Hulbert-Shearon TE, Wolfe RA, Bloembergen WE, Golper TA, Agodoa LYC, Young EW: Predialysis blood pressure and mortality risk in a national sample of maintenance hemodialysis patients. *Am J Kidney Dis* 33:507–517, 1999
42. Salem M: Hypertension in the hemodialysis population? High time for answers. *Am J Kidney Dis* 33:592–594, 1999
43. Charra B, Calemard E, Cuche M, Laurent G: Control of hypertension and prolonged survival on maintenance hemodialysis. *Nephron* 33:96–99, 1983
44. Koch M, Thomas B, Tschope W, Ritz E: Survival and predictors of death in dialysed diabetic patients. *Diabetologia* 36:1113–1117, 1993